33. The method of claim 32, wherein each of said at least two single-stranded targeting polynucleotides further comprise a homology clamp that substantially corresponds to or is substantially complementary to a preselected target DNA sequence in said zygote.

34. The method of claim 32, wherein said mammal is a farm mammal.

35. The method of claim 34, wherein said farm mammal is selected from the group consisting of cattle, sheep, pigs, horses and goats.

36. The method of claim 32, wherein said mammal is selected from the group consisting of mice, rats, rabbits, guinea pigs, hamsters and gerbils.

37. The method of claim 33, wherein the preselected target DNA sequence is selected from the group consisting of a gene or sequence encoding an ion-channel protein, a G-protein coupled receptor (GPCR), an immunoglobulin, a growth factor, an enzyme, or a milk protein.

38. The method of claim 37, wherein said milk protein gene is a lactoglobulin gene.

39. The method of claim 38, wherein said lactoglobulin gene is the α-lactoglobulin gene or the β-lactoglobulin gene.

40. The method of claim 39, wherein said modified α-lactoglobulin gene or β-lactoglobulin gene does not encode any phenylalanine residues.

41. The method of claim 32, wherein the modification of said endogenous nucleic acid is a deletion of at least one nucleotide in said endogenous nucleic acid as compared to a nucleic acid with the same sequence in a cell or mammal of the species from which the transgenic mammal is derived.

42. The method of claim 32, wherein the modification is a disruption by an insertion sequence in said endogenous nucleic acid as compared to a nucleic acid with the same sequence in a cell or mammal of the species from which the transgenic mammal is derived.

43. The method of claim 42, wherein said insertion sequence is a polylinker sequence.

44. The method of claim 42, wherein said insertion sequence is a reporter gene.

45. The method of claim 44, wherein said reporter gene is selected from the group consisting of a luciferase gene, a β-galactosidase gene and green fluorescent protein (GFP), blue fluorescent protein (BFP), red fluorescent protein (RFP) and yellow fluorescent protein (YFP).

46. The method of claim 42, wherein said insertion sequence is selected from the group consisting of a gene encoding human lysozyme, human growth hormone, human serum albumin, human globin, a human immunoglobulin, and a human enzyme.

47. The method of claim 46, wherein said human enzyme is α-1 antitrypsin.

48. The method of claim 46, wherein said human enzyme is anti-thrombin III.

49. The method of claim 46, wherein said human enzyme gene does not encode any phenylalanine residues.

50. The method of claim 42, wherein said insertion sequence is selected from the group consisting of a human gene under control of its endogenous promoter, a modified endogenous regulatory element for an endogenous gene, a transcriptional regulation cassette and a dimerizing sequence.

51. The method of claim 50, wherein said endogenous regulatory element is disrupted by deletion of at least one nucleotide.

52. The method of claim 50, wherein said regulatory element is disrupted by an insertion sequence.

53. The method of claim 37, wherein said enzyme is a sugar transferase enzyme.

54. The method of claim 53, wherein said sugar transferase enzyme is α-galactosyl transferase.

55. The method of claim 54, wherein said α-galactosyl transferase gene is disrupted by deletion of at least one nucleotide.

56. The method of claim 54, wherein said α-galactosyl transferase gene is disrupted by an insertion sequence.

57. The method of claim 56, wherein said insertion sequence is a hormone receptor gene.

58. The method of claim 56, wherein said insertion sequence is a viral receptor gene.

59. The method of claim 56, wherein said insertion sequence is a G-protein coupled receptor gene.

60. The method of claim 32, wherein the modification in said endogenous nucleic acid is selected from the group consisting of the substitution of at least one nucleotide as compared to a nucleic acid with the same sequence in a wild-type cell or mammal of the species from which the transgenic mammal is derived, an insertion of a polylinker sequence, and a deletion of at

least one nucleotide as compared to a nucleic acid with the same sequence in a wild-type cell or mammal of the species from which the transgenic mammal is derived.

61. The method of claim 60, wherein said endogenous nucleic acid is disrupted by deletion of at least one nucleotide as compared to a nucleic acid with the same sequence in a wild-type cell or mammal of the species from which the transgenic mammal is derived.

62. The method of claim 60, wherein said endogenous nucleic acid is disrupted by an insertion comprising a polylinker sequence.

63. The method of claim 32, wherein said female mammal produces at least one mammal that expresses a modified protein encoded by said modified endogenous nucleic acid.

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64. The method of claim 32, wherein said mammalian zygote is not from mouse.

65. The method of claim 34, wherein said endogenous nucleic acid is selected from the group consisting of a gene or sequence encoding an ion-channel protein, a G-protein coupled receptor (GPCR), an immunoglobulin, a growth factor, an enzyme, or a milk protein, and wherein said disruption comprises the deletion of at least one nucleotide as compared to the same gene or sequence in a wild-type cell or mammal of the species from which the transgenic farm mammal is derived.

66. The method of claim 35, wherein said endogenous nucleic acid is selected from the group consisting of a gene or sequence encoding an ion-channel protein, a G-protein coupled receptor (GPCR), an immunoglobulin, a growth factor, an enzyme, or a milk protein, and wherein said disruption comprises the insertion of a polylinker sequence as compared to the same gene or sequence in a wild-type cell or mammal of the species from which the transgenic farm mammal is derived.